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ORIGINAL ARTICLE

Influence of previous myocardial infarction site on in-hospital outcome after primary percutaneous coronary intervention for repeat myocardial infarction

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Summary
Background: Recurrent acute myocardial infarction (AMI) is a disastrous condition with high in-hospital morbidity and mortality. However, the relation between location of previous myocardial infarction (MI) and in-hospital outcome in repeat-AMI patients undergoing primary percutaneous coronary intervention (PCI) remains unclear.
Methods and results: Using the AMI-Kyoto Multi-Center Risk Study database, clinical background, angiographic findings, results of primary PCI, and in-hospital prognosis were retrospectively compared between primary PCI-treated AMI patients with previous anterior MI (anterior group,

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$n = 151$) and those with previous non-anterior MI (non-anterior group, $n = 157$). Clinical backgrounds, angiographic findings, results of primary PCI, and in-hospital outcome did not differ significantly between the two groups. On multivariate analysis, Killip class ≥3 at admission, number of diseased vessels ≥2 or diseased left main trunk at initial coronary angiography, and age were the independent predictors of in-hospital mortality in the recurrent-AMI patients, but not the anterior location of previous MI.

Conclusions: These results suggest that among recurrent-AMI patients undergoing primary PCI, in-hospital prognosis mostly depends on the severity of acute heart failure at the onset and the residual myocardial ischemia rather than previous MI sites.

Introduction

Recurrent acute myocardial infarction (AMI) is a disastrous condition with high in-hospital morbidity and mortality, which can frequently result from co-existence of multi-vessel disease, severely impaired left ventricular function, or shock states. Primary percutaneous coronary intervention (PCI) is now established as a first-line therapeutic strategy for patients with AMI and accumulating evidence has indicated that primary PCI could ameliorate the prognosis in AMI patients complicated with cardiogenic shock [1—4]. Recently, we have shown that repeat-AMI patients undergoing primary PCI had higher prevalence of Killip class ≥3 at admission, larger number of diseased vessels at initial coronary angiography (CAG), and a significantly higher in-hospital mortality rate than first-AMI patients [5]. However, data regarding repeat-AMI patients undergoing primary PCI have been limited and to our best knowledge, the relation between location of previous myocardial infarction (MI) and in-hospital outcome in repeat-AMI patients undergoing primary PCI has never been investigated. The AMI-Kyoto Multi-Center Risk Study, a large multicenter observational study in which 16 collaborating hospitals in Kyoto Prefecture have collected demographic, procedural, and outcome data on AMI patients, was established in 2000 in order to analyze these data and establish an emergency-hospital network for heart diseases in Kyoto [5—8]. The purpose of the present study is therefore to compare in-hospital prognosis in primary PCI-treated recurrent-AMI patients having previous anterior MI with those of recurrent-AMI patients having previous non-anterior MI, using data from the AMI-Kyoto Multi-Center Risk Study.

Methods

Patient population

From January 2000 to December 2007, 3010 consecutive patients with a diagnosis of AMI, who were admitted to AMI-Kyoto Multi-Center Risk Study Group Hospitals within 1 week after the onset of AMI, were enrolled in the present study (Fig. 1). Of these, 414 patients had previous MI, and 314 out of the 414 patients with previous MI received primary PCI, of whom data on clinical background were available in 308. Previous MI and the sites of that were identified by medical history and echocardiographic findings. Previous anterior MI was defined as antecedent MI in anterior site or multiple sites including anterior site. We retrospectively compared clinical background, coronary risk factors, angiographic findings, acute results of primary PCI, and in-hospital prognosis between primary PCI-treated AMI patients with previous anterior MI (anterior group, $n = 151$) and those with previous non-anterior MI (non-anterior group, $n = 157$) (Fig. 1). The diagnosis of AMI required the presence of two of the following three criteria: (1) characteristic clinical history; (2) serial changes on the electrocardiogram suggesting infarction (Q-waves) or injury (ST-segment elevations); and (3) transient increase in cardiac enzymes to more than 2-fold the normal laboratory value.

Data collection

The patients' demographic information, cardiovascular history, and risk factors (i.e. smoking, hypercholesterolemia, hypertension, and diabetes mellitus) were recorded. Hypercholesterolemia was defined as total cholesterol ≥220 mg/dl or the use of cholesterol-lowering agents; hypertension was defined as systemic blood pressure ≥140/90 mmHg or the use of antihypertensive treatment; diabetes mellitus was defined as fasting blood sugar ≥126 mg/dl or the use of specific treatment. After informed consent to participate in the AMI-Kyoto Multi-Center Risk Study was confirmed by each patient, all in-hospital data were transmitted to the center located at the Department of Cardiovascular Medicine in Kyoto Prefectural University School of Medicine for analysis. The study protocol was approved by each hospital's ethics committee.

Emergency CAG and reperfusion therapy

Emergency CAG was performed using the standard technique. The coronary flow in the infarct-related artery (IRA) was graded according to the classification used in the thrombolysis in myocardial infarction (TIMI) trial. Significant coronary artery stenosis was defined as at least a 75% reduction in the internal diameter of the right coronary arteries (RCA), left anterior descending coronary arteries (LAD), or left circumflex coronary arteries (LCx) and their major branches, or a 50% reduction in the internal diameter of the left main trunk (LMT). Non-significant stenosis was defined as coronary arterial narrowing less than a significant stenosis. Patients with either angiographically normal coronary arteries or non-significant stenosis were classified as having zero-vessel disease. Multi-vessel culprit lesions were defined

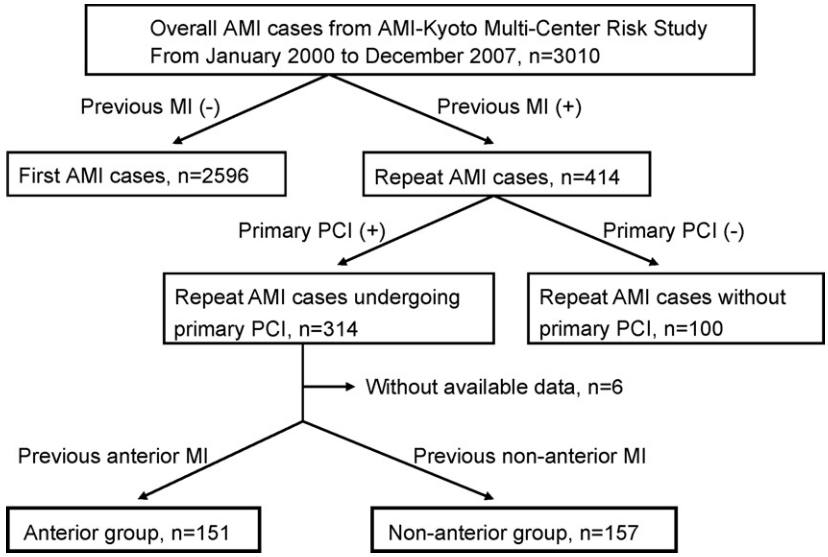

Figure 1 Flowcharts of patients. AMI, acute myocardial infarction; MI, myocardial infarction; PCI, percutaneous coronary intervention.

as simultaneous thromboses of multiple coronary arteries in the initial CAG. After the culprit lesions were ascertained by CAG, primary PCI was subsequently performed.

Statistics

Data are expressed as mean ± SD. The anterior and the non-anterior groups were compared using the chi-square test for discrete variables and unpaired Student's *t*-test for continuous variables according to standard statistical methods. The odds ratio and 95% confidence intervals assessing the risk of in-hospital death were estimated by multivariate logistic regression analysis. In the multivariate logistic regression analysis, TIMI flow grade was categorized into two groups: grade 3 and grade ≤ 2 or unknown. In all analyses, significance was accepted at $p < 0.05$. Statistical analysis was performed with a standard statistical software (StatView, version 5.0, SAS Institute Inc., Cary, NC, USA).

Results

Patient characteristics and risk factors

The clinical characteristics and risk factors in the 2 groups are summarized in Table 1. There were no significant differences in the clinical background and the prevalence of coronary risk factors between the 2 groups.

Angiographic data

Table 2 shows the emergency coronary angiographic data in the 2 groups. The anterior group tended to have culprit lesions in the LAD, compared with the non-anterior group, although the difference was not significant. The number of diseased vessels did not vary between the 2 groups.

Table 1 Clinical characteristics of the study patients (the anterior group vs. the non-anterior group). PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

	Anterior (n = 151)	Non-anterior (n = 157)	p-Value
Age (mean years ± SD)	67.1 ± 11.9	68.4 ± 13.7	0.354
Male (%)	126 (83.4)	123 (78.3)	0.256
Previous PCI (%)	68 (45.0)	85 (54.1)	0.110
Previous CABG (%)	9 (6.0)	8 (5.1)	0.740
Risk factors			
Smoking (%)	52 (34.4)	54 (34.4)	0.994
Hypercholesterolemia (%)	52 (34.4)	60 (38.2)	0.491
Hypertension (%)	65 (43.0)	71 (45.2)	0.701
Diabetes mellitus (%)	52 (34.4)	46 (29.3)	0.333
Elapsed time <24 h (%)	140 (92.7)	143 (91.1)	0.600
Killip 3/4 (%)	30 (19.9)	31 (19.7)	0.979

Table 2 Angiographic findings of the study patients. RCA, right coronary artery; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; LMT, left main trunk; SVG, saphenous vein graft.

	Anterior (n = 151)	Non-anterior (n = 157)	p-Value
Culprit lesions			
RCA (%)	45 (29.8)	73 (46.5)	0.087
LAD (%)	69 (45.7)	55 (35.0)	
LCx (%)	27 (17.9)	23 (14.6)	
LMT (%)	4 (2.6)	2 (1.3)	
Multivessels (%)	5 (3.3)	3 (1.9)	
SVG	1 (0.7)	1 (0.6)	
No. of diseased vessels			
0 (%)	0 (0.0)	0 (0.0)	0.816
1 (%)	71 (47.0)	78 (49.7)	
2 (%)	48 (31.8)	50 (31.8)	
3 (%)	28 (18.5)	27 (17.2)	
LMT (%)	4 (2.6)	2 (1.3)	

Results of coronary intervention

Table 3 shows the results of primary PCI in the two groups. Data on TIMI grade in the IRA were available in 140 of the 151 patients with previous anterior MI and in 150 of the 157 patients with previous non-anterior MI. The anterior group was more likely to have lower TIMI grade in the IRA before primary PCI, compared with the non-anterior group, although the difference was not significant (p = 0.083). The distribution of TIMI grade immediately after primary PCI did not differ significantly between the 2 groups. Frequency of coronary stents and mechanical support devices did not vary between the two groups.

Table 3 Results of coronary intervention in the study patients. TIMI, thrombolysis in myocardial infarction; IABP, intraaortic balloon pumping; PCPS, percutaneous cardiopulmonary support. Data on TIMI grade available only for 140 of the anterior group and for 150 of the non-anterior group.

	Anterior (n = 151)	Non-anterior (n = 157)	p-Value
Pre TIMI grade			
0	91 (65.0)	80 (53.3)	0.083
1	12 (8.6)	24 (16.0)	
2	20 (14.3)	19 (12.7)	
3	17 (12.1)	27 (18.0)	
Post TIMI grade			
0	1 (0.7)	5 (3.3)	0.311
1	3 (2.1)	1 (0.7)	
2	7 (5.0)	8 (5.3)	
3	129 (92.1)	136 (90.7)	
Stent (%)	114 (75.5)	116 (73.9)	0.745
IABP (%)	35 (23.2)	30 (19.1)	0.381
PCPS (%)	2 (1.3)	5 (3.2)	0.273
Pacing (%)	13 (8.6)	14 (8.9)	0.924

In-hospital outcomes

Table 4 shows the in-hospital prognosis in the 2 groups. There were no significant differences in in-hospital overall mortality as well as in-hospital cardiac-related mortality between the 2 groups. The anterior group was more likely to have death ascribed to heart failure, compared with the non-anterior group, although the difference was not significant. The length of hospital stay and the maximum creatine phosphokinase concentration did not differ between the two groups. In order to assess the contribution of clinical background, risk factors, angiographic findings, and results of primary PCI, multivariate logistic regression analysis using all available variables (age, gender, smoking, hypercholesterolemia, hypertension, diabetes mellitus, multi-vessel or LMT as culprit lesions, number of diseased vessels ≥2 or diseased LMT, stent usage, elapsed time <24 h, Killip class ≥3 at admission, TIMI 3 flow before/after primary PCI, previous anterior MI) was developed for overall death during hospitalization in the study population (Table 5). Killip class ≥3 at admission, number of diseased vessels ≥2, or diseased LMT at initial CAG, and age were the independent predictors of in-hospital mortality, but the anterior location of previous MI was not.

Discussion

The major findings of the present multicenter study are as follows: (1) among patients with recurrent AMI undergoing primary PCI, the in-hospital outcome was similar for the patients with previous anterior MI and the patients with previous non-anterior MI. (2) According to the results of multivariate analysis, Killip class ≥3 at admission, number of diseased vessels ≥2 or diseased LMT at initial CAG, and age were independent predictors of in-hospital death, but previous anterior MI was not.

This study was the first to investigate the impact of previous MI location on the in-hospital outcome in patients with recurrent AMI undergoing primary PCI. There have been few studies of patients with repeat AMI undergoing primary PCI, but we recently reported that such patients receiving primary PCI had a higher prevalence of Killip class ≥3 at admission, more diseased vessels, more often needed intraaortic balloon pump support during PCI, and had a significantly higher in-hospital mortality rate than patients with their first AMI [5]. Repeat-AMI patients tend to have poor left ventricular function compared with first-AMI patients, and we have therefore hypothesized that patients with prior anterior MI (who have more severe left ventricular dysfunction) might have a worse in-hospital outcome than patients with previous non-anterior MI. Therefore, we focused on the influence of the previous MI site on the in-hospital outcome in repeat-AMI patients undergoing primary PCI. Unexpectedly, this study showed that the clinical background, angiographic findings, results of primary PCI, and in-hospital outcome after PCI did not differ significantly between recurrent-AMI patients with previous anterior MI and those with previous non-anterior MI. In addition, although detailed data regarding left ventricular function were lacking, the frequency of a Killip class ≥3 at admission and the use of mechanical support devices did

Table 4 In-hospital outcomes in the study patients. CK, creatine phosphokinase; Vf, ventricular fibrillation. Data on max CK available only for 149 of the anterior group and for 149 of the non-anterior group.

	Anterior (n = 151)	Non-anterior (n = 157)	p-Value
Length of hospital stay (days)	22.9 ± 19.0	23.4 ± 19.4	0.825
max CK (IU/L)	2649.3 ± 2887.4	2727.5 ± 4008.3	0.847
Death (%)	21 (13.9)	23 (14.6)	0.852
Cardiac-related (%)	18 (11.9)	14 (8.9)	0.388
Shock	6	5	0.709
Heart failure	9	3	0.066
Rupture	1	3	0.333
Vf	2	3	0.684
Noncardiac-related (%)	3 (2.0)	9 (5.7)	0.089

Table 5 Predictors of in-hospital mortality in the study patients (multivariate logistic regression analysis). OR, odds ratio; CI, confidence intervals; LMT, left main trunk; TIMI, thrombolysis in myocardial infarction; PCI, percutaneous coronary intervention.

	OR	95% CI	p-Value
Killip 3/4	5.982	2.772–12.911	<0.0001
No. of diseased vessels ≥2 or LMT	2.260	1.005–5.082	0.0486
Age	1.048	1.010–1.088	0.0137
Multi-vessels or LMT as culprit	1.469	0.390–5.528	0.5695
TIMI 3 before PCI	1.169	0.441–3.099	0.7539
TIMI 3 after PCI	0.469	0.169–1.305	0.1471
Elapsed time <24 h	0.603	0.202–1.803	0.3654
Stent usage	1.268	0.516–3.117	0.6045
Previous anterior MI	0.960	0.461–1.996	0.9122

not vary between these groups. However, the recurrent-AMI patients with previous anterior MI were more likely to suffer from death due to heart failure than the recurrent-AMI patients with previous non-anterior MI, although the difference was not significant.

The influence of the location of MI on the prognosis remains controversial. A previous study indicated that patients with anterior MI had a higher long-term mortality rate than patients with inferior MI, while another study showed that the location of MI did not influence the long-term prognosis [9,10]. In contrast, another recent report from Gomez and colleagues demonstrated that among patients with a very low ejection fraction, those with inferior MI had a worse prognosis than those with anterior MI [11]. In addition, a recent Japanese study has shown that patients with previous inferior MI undergoing isolated coronary artery bypass grafting have significantly higher postoperative morbidity and mortality rates than patients with previous anterior MI [12]. The authors of these reports speculated that right ventricular dysfunction or ischemic mitral regurgitation might play a critical role in the worse outcome of patients with previous inferior MI. Although we did not obtain data regarding right ventricular function and mitral regurgitation in the present study, there is a possibility that these factors might have contributed to the similar in-hospital prognosis of AMI patients with previous anterior MI and those with previous non-anterior MI. On the contrary, based on our results of multivariate analysis, Killip class ≥3 at admission, number of diseased vessels ≥2 or diseased LMT at initial CAG were independent predictors of in-hospital death, but previous anterior MI was not, suggesting that in-hospital prognosis of repeat-MI patients mostly depends upon the severity of acute heart failure at the onset and the residual myocardial ischemia rather than previous MI sites.

In the present study, recurrent-AMI patients with previous anterior MI were more likely to have culprit lesions in the LAD than recurrent-AMI patients with previous non-anterior MI, although the difference was not significant. We cannot explain this trend precisely, but recent reports have indicated that, in addition to the culprit lesion, multiple vulnerable plaques can be detected in the culprit artery and the non-culprit arteries of patients with acute coronary syndrome by intravascular ultrasound and angioscopy [13,14]. Thus, there might be no reason for the culprit lesion of patients with recurrent AMI to occur in a specific coronary artery. In addition, there is a possibility that patients with broad anterior infarction at their previous MI and recurrent AMI in the RCA or LCx territory might suffer from cardiopulmonary arrest or sudden death before reaching hospital and thus could be excluded from our database.

The present study showed that recurrent-AMI patients with previous anterior MI were more likely to have worse flow (a lower TIMI grade) in the IRA before primary PCI than recurrent-AMI patients with previous non-anterior MI, although the difference was not significant. According to a previous study that compared patients with or without TIMI 3 flow prior to primary PCI, patients with TIMI 3 flow were less likely to have signs of heart failure and left ventricular dysfunction during emergency CAG [15]. In addition, other previous studies have indicated that a left ventricular ejection fraction <50%, cardiogenic shock, and increased heart rate were independent predictors of final TIMI flow $\leq$2 [16—18]. Another recent Japanese report pointed out that acute hyperglycemia on admission, which might represent hemodynamic instability or heart failure through the release of catecholamine and adrenal corticosteroids, was independently associated with the higher corrected TIMI frame counts after primary stenting [19]. These findings have suggested that left ventricular dysfunction might be closely related to prior lower flow as well as final lower flow in the IRA after primary PCI.

Limitations

First, this was a retrospective observational analysis of a small number of patients. Second, data on the clinical and angiographic features at the time of previous PCI were not available for all repeat-AMI patients undergoing primary PCI. Third, we did not assess left ventricular function and the door-to-balloon time, which might be predictors of in-hospital death. In the present study, Killip class $\geq$3 at admission was the most powerful predictor of hospital mortality after repeat AMI, and left ventricular dysfunction might therefore influence the in-hospital prognosis in this patient population. Fourth, data regarding the interval between the previous MI and recurrent AMI were missing. Fifth, ''ST elevation MI'' was not discriminated from ''non-ST elevation MI''.

Conclusion

The present study provides evidence that among recurrent-AMI patients undergoing primary PCI, in-hospital prognosis mostly depends on the severity of acute heart failure at the onset and the residual myocardial ischemia rather than previous MI sites. However, the small size of the study population as well as the lack of data regarding left ventricular function are major limitations, so a larger and more detailed study should be performed to confirm our findings.

Appendix A.

The following institutions and principal investigators participated in the present study as the AMI-Kyoto Multi-Center Risk Study Group: Kyoto City Hospital: Matsubara K, Shima M, Kiyama M; Kyoto Kidugawa Hospital: Miyanaga H, Nakagawa T, Matsui H, Kunieda Y; Kyoto Second Red Cross Hospital: Fujita H, Tanaka T, Inoue K, Matsuo A, Tsubakimoto Y; Social Insurance Kyoto Hospital: Yamada C, Oda Y, Tanabe S; Nantan General Hospital: Tatsumi T, Keira N, Nishikawa S, Nomura T; Ayabe Municipal Hospital: Shiga K, Kohno Y, Adachi Y, Yokoi H; Kameoka Municipal Hospital: Kuriyama T, Matsuo R; Maizuru Medical Center: Harada Y, Hikosaka T, Nakagami T, Nakajima N; Kyoto Saiseikai Hospital: Yamahara Y, Ishibashi K; Gakkentoshi Hospital: Sakai R, Akashi K; Aiseikai Yamashina Hospital: Katamura M, Yamamoto T; Kouseikai Takeda Hospital: Kinoshita N, Irie H, Nakamura R; Fukuchiyama Municipal Hospital: Nishio M, Sakamoto T, Hayashi H, Matsunaga S; Kyoto Prefectural Yosanoumi Hospital: Kimura S, Isodono K, Honsho S, Tagawa M; Kyoto First Red Cross Hospital: Matsui A, Ariyoshi M, Kimura M; Kyoto Prefectural University School of Medicine: Takahashi T, Shiraishi H, Yamano T.

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